EFFICACY TESTING OF VERTEBRATE PEST CONTROL AGENTS

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ABSTRACT: Justification for efficacy testing is provided under the present FIFRA, and the PR notice 70-15 requirements. In addition, the Pure Food and Drug Laws, the Delaney Amendment and other laws effect the requirements of registration of all economic poisons. Basic preliminary registration information such as toxicological data, chemistry data, must be provided on all chemicals proposed as economic poisons. Once the basic chemical and toxicological properties have been determined, the applicant must consider basic efficacy requirements. Efficacy requirements should consider the effects of particle size and shape, taste and odor, impurities, diluents, stickers and solvents, volatility, mode of action, and other factors such as age, sex, species, characteristics and ambient temperatures.

Specific studies, however, will vary with the intended use of the product and the target species involved. Field testing is required for all proposed products under actual field situations. These tests logically follow appropriate laboratory tests.

The risk-benefit ratio is defined as a ratio of hazards to nontarget organisms as compared to the benefits resulting from the products use. At present, this ratio has not been made a part of the registration procedure, but has been used in adverse action.

The justification for a presentation on efficacy testing is provided in the Federal Insecticide, Fungicide, and Rodenticide Act, the Federal law now administered by EPA, Pesticides Regulation Division. This law states in the "Procedure for Registration"[1] that the Director may request ... "a full description of the tests made and the results thereof upon which the claims for the economic poison are based, together with such other information as may be necessary to assure compliance with the Act." Also "... the applicant for registration is responsible for the accuracy and completeness of all information submitted in connection with his application for registration of an economic poison."[1]

The Act further states "If it does not appear ... that the article is such as to warrant the proposed claims or if the article and its labeling and other material required to be submitted do not comply with the provisions of the Act, 'he' (the Director or his delegate) shall notify the applicant for registration of the manner in which the article, labeling or other material required to be submitted fail to comply with the Act ...."[2]

In addition, the requirements of PR Notice 70-15, the request by industry and government to publish registration requirements, the requirements of the Pure Food and Drug Law, the Delaney Amendment and other laws require more data on more products than ever before. This is especially true in respect to vertebrate pest control chemicals.

Before going into a discussion of efficacy testing it would be well to understand some of the earlier stages of a chemical's development. Some of the information necessary at the early stages of development may overlap some efficacy studies.

Certain basic preliminary data or preliminary information must be provided on all chemicals proposed as economic poisons. Such information is to include, but is not limited to (1) chemistry requirements; the physical-chemical properties such as melting point, boiling point, vapor pressure, density or specific gravity, hydrolysis rate, soluability in various solvents, stability, physical state, color, odor, and composition giving the impurities. In addition, information on the basic manufacturing process and methods of impurity assessment may also be required.

(2) Basic toxicological requirements include, but are not limited to, acute toxicities (acute oral, acute dermal, inhalation[3], primary skin irritation, and eye irritation) subacute toxicity and exposure studies.

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[1] Title 7, Chapter III, Pt. 362 of the FIFRA, Aug. 29, 1964 (Sect. 362.10(c) & (f)
[2] 61 stat. 163; 7 U.S.C. 135-135k. The FIFRA, Oct. 1, 1964 (Sect. 4(c))
[3] May be required depending on the formulation and proposed pattern of use.

Anyone who may use this presentation as a reference for future registration must realize that the exact requirements of data for any chemical or proposed formulation will depend on the final formulation, the pattern of use, and the nature or hazards inherent in the chemical itself. A general discussion simply cannot provide all the specific requirements for a specific chemical proposed for a specific use.

EFFICACY REQUIREMENTS

Once the basic chemical and toxicological properties have been determined, a manufacturer must consider appropriate basic efficacy studies. These studies will vary according to the intended use of the chemical and the intended target species.

It is recognized that the albino laboratory rat and mouse are invaluable in the screening and study of chemicals proposed as rodenticides. Nevertheless, acceptable evidence of efficacy in the final stages of study must include the exact animal form against which the product is to be used.

As in the preliminary data requirements there are some general studies which are applicable to vertebrate pesticides as a group. These include, but are not limited to, the effects of particle size and shape, taste and odor, impurities, diluents, stickers and solvents, volatility, mode of action, and other factors such as age, sex, species characteristics, and temperature.

Effects of particle size and shape on acceptance and utility of the chemical can produce variation in results, for example the particle size has a very great effect on the toxicity of arsenic trioxide (McDougall 1944). Particle shape may affect the choice of diluent.

Taste and odor obviously affect the acceptance of a chemical which may be proposed as bait. Strychnine, for example, is not acceptable as a commensal rat poison because of the lack of efficacy due in part to its bitter taste. Odor, likewise, may affect acceptance of a chemical as a bait. Once an animal has had a bad experience associated with a particular odor, that animal may refuse similar bait materials with the same odor.

Impurities often effect acceptance and may effect the toxicity. Impurities may impart taste, odor or other characteristics which may make a bait unpalatable (Bowerman and Brooks 1972).

Diluents, solvents, and stickers affect the utility of a chemical since they may impart undesirable characteristics of taste, rate of release in a target animal, or sloughing off in transit.

Volatility of a chemical may have several effects. If the chemical is highly volatile it may dissipate before it can be effective. It may transfer from the point of application to some other location where it may not be desirable and increase the hazard of its use.

Mode and rate of reaction may not directly affect the efficacy of a chemical but may certainly have an effect on its registration. If the chemical is likely to cause irritation, tumors, etc., it may be hazardous in use. The rate of reaction may directly affect the efficacy of the product. If the material in a bait reacts too rapidly it is probable that there will be acceptance problems. If the reaction is too slow it may not be effective even though it may be well accepted.

Other factors, to be considered in efficacy requirements are sex, age, susceptibility, temperature effects, species characteristics, etc. The susceptibility of different sexes is well documented but one of the best examples is red squill. Red squill is nearly two to two and one half times more toxic to female rats (Rattus norvegicus) than it is to male rats. Species susceptibility is also documented many times, such as with ANTU (alpha-napthylthiourea). ANTU has an LD_{50} of 8 mg/kg to Norway rats (Rattus norvegicus) and LD_{50} of 220 mg/kg for the roof rat (Rattus rattus). The differences in susceptibility need not be of this magnitude to result in changed wording and modified claims on the label.

SPECIFIC STUDIES

As indicated earlier, specific studies will vary depending on the intended use of the chemical and must be conducted with the target species.

At this point individuals associated with the studies should be thoroughly familiar with the life habits and behaviorisms of the test species. The anticipated method of field application should be kept in mind when designing tests under cage or captive conditions.

Studies with chemicals to be used as baits and taste repellents should include, in addition to acute and subacute toxicities, such things as bait and chemical acceptance, reacceptance, the individual and group animal reactions, the time in the life cycle and daily cycle for maximum effect, sex effect, age effect, duration of the effect (especially repellents and chemosterilants), and other studies which may indicate the reaction of the target species under normal conditions of use.

Chemicals proposed for use as tactile and odor repellents and dermal toxicants should include, in addition to acute oral and dermal toxicities, subacute oral and dermal toxicities, skin and eye irritation, such things as visual, odor and/or taste responses by individuals and groups of test animals, behavioral changes, duration of the changes or effects, dose effect, sensory adaptation and/or fatigue interval, stability of responses under strong pressure, intervals of application, temperature variation affects, sex and age differentiation in response, life cycle and daily cycle effects, etc.

Speciality products such as fish toxicants and molluscicides require similar tests which will indicate their efficacy under various water quality, temperature, and pH conditions. In addition the chemical's behavior in water, the degradation time and products and their behavior should be studied as well as a detoxifying agent.

Special claims or items require tests which will reflect their efficacy.

Chemicals applied on or around plants, on seeds, and other surfaces, must be supported by data showing phytotoxicity, staining characteristics, germination effects, or any other undesirable characteristics. If a chemical is to be applied to food or feed crops, data must be submitted showing crop residues, degradation time and products, etc. And all chemicals proposed as vertebrate pest control products must have data showing the hazard to nontarget species.

FIELD TESTING

After the laboratory testing indicated above, all proposed products and formulations must be tested under conditions of actual use in field situations. The factors of inter- and intra- species behaviorisms and the impact of environmental factors are so complex that cage testing simply cannot suffice.

Field testing therefore, should be conducted with sufficient replications to indicate the variations in the habitat of the target species throughout its normal range. Particular attention should be given to individual and group behavioral responses, degree and duration of the response, responses of nontarget organisms, the acceptability of the bait or other materials, any undesirable responses and any other factors which may affect the efficacy and utility of the product. Field testing without controls or established base lines of activity are open to speculation.

RISK - BENEFIT RATIO

There is one more significant factor which may affect the registration of a chemical or use. That is the Risk - Benefit Ratio. The Risk - Benefit Ratio involves evaluation of the hazards to nontarget organisms resulting from a particular chemical use compared to benefits resulting from the use. While this has not been made a requirement of registration for vertebrate pest control products it has played a significant role in actions taken against several chemicals and uses. My purpose in mentioning it here, is because I feel you should be aware of this particular aspect. It is not a requirement for registration but it is very definitely an important consideration in such registration.

SUMMARY

The present FIFRA states that data may be requested at the discretion of the Director. Data submitted in support of registration must support all claims made in the labeling. The data requirements discussed generally fall into three catagories--preliminary laboratory studies, advanced laboratory studies and field studies. The exact procedure followed will depend upon the nature of the chemical, the target species, and the pattern of use. Individuals conducting such studies must be familiar with the target animals' habits and environment. Field testing must be conducted with each chemical, use pattern, and target species. Hazards to the environment should be considered similarly.

LITERATURE CITED

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